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Case report

Lipoblastoma: A rare soft palate mass

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ABSTRACT

Lipoblastomas are rare benign tumors originating from embryonic fat cells that continue to proliferate in the postnatal period. Most tumors occur around age three and are found predominantly in the extremities and trunk. Less than fifteen cases have been reported in the head and neck region. We present a case of lipoblastoma arising in the soft palate, a site that has not been previously reported. By doing so, we hope to promote awareness of this pathology and emphasize the importance of using histological and cytogenetic analysis to obtain the correct diagnosis.

1. Introduction

Lipoblastomas are rare, benign, adipose tumors that are composed of embryonic fat tissue of different maturation stages ranging from prelipoblasts to lipoblasts and finally mature lipocytes. These tumors are extremely rare and comprise 2% of pediatric soft tissue tumors [1]. Lipoblastomas present in infancy and early childhood and can even be present at birth. Perlis et al. report that 80% of lipoblastomas present in children before 3 years of age, however there are exceptional reports of lipoblastomas in adults [2]. The majority of the lesions involve the extremities and the trunk. Few cases have been reported in the head and neck region [1,2].

Histologically, lipoblastomas have a multilobular pattern composed of adipocytes at different maturation stages divided by mesenchymal areas with a loose myxoid matrix and connective tissue septa [3]. Sometimes, lipoblasts may not be found and the matrix might have a plexiform vascular pattern, making the differentiation between lipoblastomas and lipomas or myxoid liposarcoma difficult. In such cases, additional cytogenetic analysis is helpful. Forty-three abnormal karyotypes for lipoblastomas have been reported in the literature [4]. In all cases, chromosome 8 anomalies including rearrangements in number or structure have been described [4]. Approximately 80% of those cases have shown clustering of breakpoints to the 8q11-13 region [5]. These chromosomal rearrangements target the *Pleomorphic adenoma gene-1* (*PLAG1*) located on chromosome 8q12. The PLAG1 oncogene becomes overexpressed by a promoter-swapping event. Two different genes have been found to fuse with PLAG1 and promote the upregulation of the tumor cells: *Hyaluronan synthase 2* (*HAS2*) at 8q24.1 and *Collagen type I alpha-2* (*COL1A2*) at 7q22, forming *HAS2-PLAG1* and *COL1A2-PLAG1* [6–8]. Subsequently, it is thought that this promoter fusion produces the induction of growth factors such as *insulin-like growth factor-2* (*IGF2*) and its receptor, *insulin-like growth factor-1 receptor* (*IGF1R*) [9,10]. This receptor activates downstream substrates, resulting in activation of the *Mitogen-activated protein protein kinase* (*MAPK*) signaling pathway and the *Phosphoinositide 3-kinase* (*PI-3*)/*AKT* pathway, which are critical pathways in regulating proliferation and apoptosis in human cells [11].

We report the first known case of a soft palate lipoblastoma in an 8-year-old girl. Additionally, we present one of the first descriptions of a lipoblastoma lacking the characteristic rearrangement in chromosome 8, but having abnormalities more frequently encountered in other lipomatous and soft tissue tumors, such as a translocation between chromosomes 1 and 2 and the presence of ring and marker chromosomes.

2. Report of case

An 8-year-old girl initially presented with a right soft palate mass. Computed tomography evaluation showed a 1.5 cm × 3.5 cm fat attenuated mass in the soft palate. It extended into the oropharynx and displaced the uvula to the contralateral side (Fig. 1). Given these radiological findings, the lesion was believed to be a lipoma and the patient was taken to the operating room

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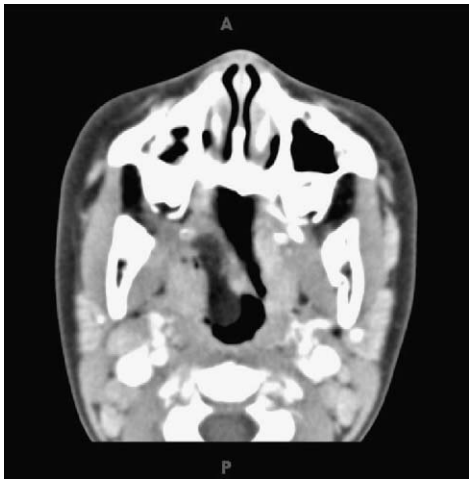

Fig. 1. Initial axial CT scan prior to the first surgical resection.

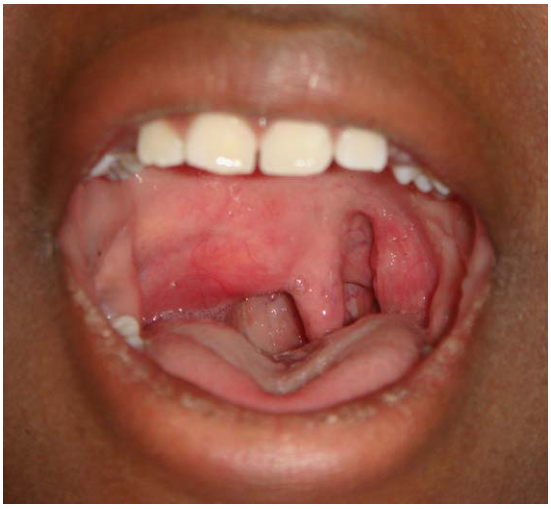

Fig. 2. Right soft palate mass extending medially from the tonsillar fossa and deviating the uvula to the left.

where a local excision of the mass was performed. The pathology evaluation demonstrated a lobular configuration with fibrous septa and frequent peripheral lipoblasts compatible with a maturing lipoblastoma. After her surgery, the patient was lost to follow-up.

Three years later the patient returned with recurrence of the mass. Her symptoms included right nasal obstruction, snoring, choking and a gagging sensation. There were no witnessed apneas and the patient had a normal voice without hypo or hyper-nasality. On examination, there was a large right soft palate mass obstructing the right tonsil and deviating the uvula to the left (Fig. 2). On palpation, the mass was soft and non-tender. There was no cervical lymphadenopathy or other lesions noted in the head and neck exam. A magnetic resonance imaging (MRI) study with gadolinium was performed which showed a 1.5 cm $\times$ 3.2 cm $\times$ 2.7 cm fatty lesion of the right soft palate extending laterally to the right tonsil (Fig. 3). The patient was taken back to the operating room where a wide local excision of the lesion was performed. A right tonsillectomy was also performed to ensure clear margins. Frozen sections from all margins were negative for tumor.

The final pathology showed again a lobular configuration of the lesion with fibrous septa and frequent immature elements (lipoblasts) at the periphery of the lobules, consistent with a maturing lipoblastoma (Fig. 4). Previous amniocentesis that the mother underwent when she was pregnant showed that the patient's karyotype had normal chromosomes (46 X,X). A cytogenetic analysis of the lesion was performed. Ten metaphases were analyzed and one cell line was observed. The abnormalities in the detected clone (10/10 cells) included a derivative chromosome 2 formed by an unbalanced translocation between the short arm of chromosome 1 and the long arm of chromosome 2; 3–6 ring chromosomes; and a marker chromosome of unknown origin. Therefore, the karyotype of tumor cells described according to the International System for Human Cytogenetic Nomenclature (ISCN) 2005 [12] was: 49–52 XX,der(2)t(1;2)(p31;q37), +3- 6r, +mar. Given the association of lipoblastomas and abnormalities in chromosome 8, interphase and methaphase fluorescence in situ hybridization (FISH) were performed revealing no chromosomal abnormalities.

The postoperative course was uneventful. The patient was followed clinically at 1, 3 and 6 months. A postoperative MRI obtained at 6 months showed no evidence of recurrence (Fig. 5). The patient was again lost to follow-up after the 6-month postoperative visit.

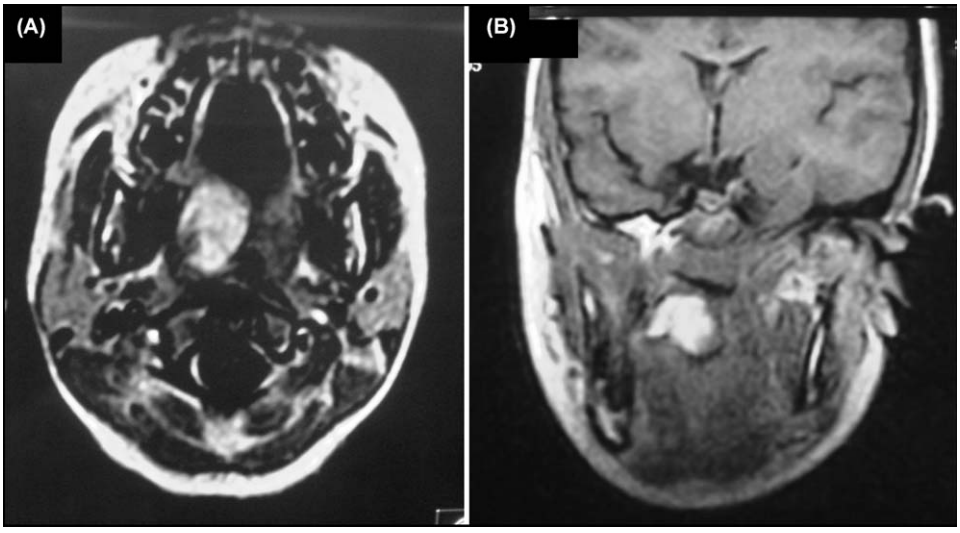

Fig. 3. MRI images of recurrent lipoblastoma. (A) Shows the axial view of a T1 waited image without contrast; the mass is hyperintense occupying the right soft palate, tonsillar fossa and a portion of nasopharynx. (B) Shows a coronal view showing extension into the right lateral pharyngeal wall.

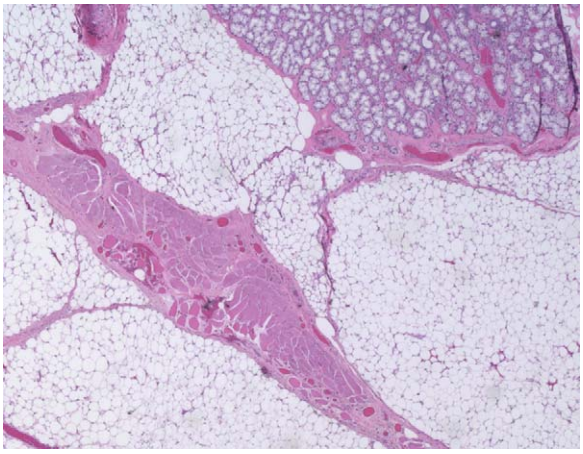

Fig. 4. Photomicrograph of recurrent lipoblastoma specimen (Hematoxylin-Eosin stain 10× magnification). The lesion has a lobular configuration with fibrous septa and immature elements in the periphery of the lobules. These features are characteristic of the classic lipoblastoma subtype morphology.

3. Discussion

Lipoblastomas are rare, benign, adipose tumors that present in early childhood and most commonly occur on the extremities and the trunk. To our knowledge, this is the first case of a lipoblastoma involving the soft palate. The typical presentation for lipoblastoma is a painless, enlarging soft tissue mass. Two types of lipoblastoma exist: a well-defined, encapsulated form simply called lipoblastoma, and a diffuse, ill-margined form called lipoblastomatosis. Lipoblastomatosis lesions are considered to have a slightly higher recurrence rate than lipoblastomas. Both types can exhibit rapid growth and generate mass effect on surrounding structures [13]. Rare cases of lipoblastoma growing rapidly enough to obstruct the airway have been reported [14].

Pathologic analysis generally establishes the definitive diagnosis of lipoblastomas. A subclassification of lipoblastomas based on histological findings has been proposed: (1) the classic type, where a myxoid matrix composed of spindle cells, stellate mesenchymal cells, and intercellular mucin is seen in the background of an adipocytic component; (2) myxoid lipoblastomas where marked interstitial mucin is found; (3) lipoma-like lipoblastomas missing the myxoid component and formed mainly of mature adipocytes; (4) hibernoma-like lipoblastomas lacking a myxoid component and made principally of multi-vacuolated lipoblasts [10]. Occasionally, morphologic studies are insufficient to obtain a definitive diagnosis. In such cases, additional genetic analysis might be necessary to distinguish lipomatous tumors, particularly when differentiating a benign from a malignant lesion given their distinct prognostic implications.

3.1. Genetics characteristics of lipomatous tumors

Genetics are particularly relevant when the specimen lacks the typical lipoblasts or when atypical morphologic characteristics are present. Most lipomatous tumors have characteristic chromosomal rearrangements, affecting the expression or regulation of specific proteins, making cytogenetics an important tool for diagnosis.

3.1.1. Lipoblastomas

Upregulation of the *PLAG1* transcription factor by chromosomal rearrangements, targeting chromosomal region 8q11-13, is a common event in lipoblastomas [15]. Some lipoblastomas have trisomy of chromosome 8 but lack a specific translocation [16]. Of note, rearrangements on *PLAG1* have been reported in all subtypes of lipoblastomas [17].

3.1.2. Myxoid liposarcomas

In well-differentiated liposarcomas, the most common chromosomal abnormalities are supernumerary ring and giant marker chromosomes. Generally, amplified sequences from 12q are found in these aberrant chromosomes [18]. Rearrangements of the *DNA damage-inducible transcript 3* (*DDIT3 or CHOP*) gene due to chromosomal abnormalities in 12q13 are common in liposarcomas [19]. Two different genes have been reported to fuse with *CHOP* giving rise to transcriptional upregulators: *CHOP/FUS* fusion gene, in 16p11, and *CHOP/Ewing sarcoma breakpoint region 1* (*EWS*), in 22q12.9. These oncoproteins affect the expression of genes related to adipocytic differentiation [20]. *Mouse double minute 2 homolog* (*MDM2*) is another oncogene altered in liposarcomas. *MDM2* binds

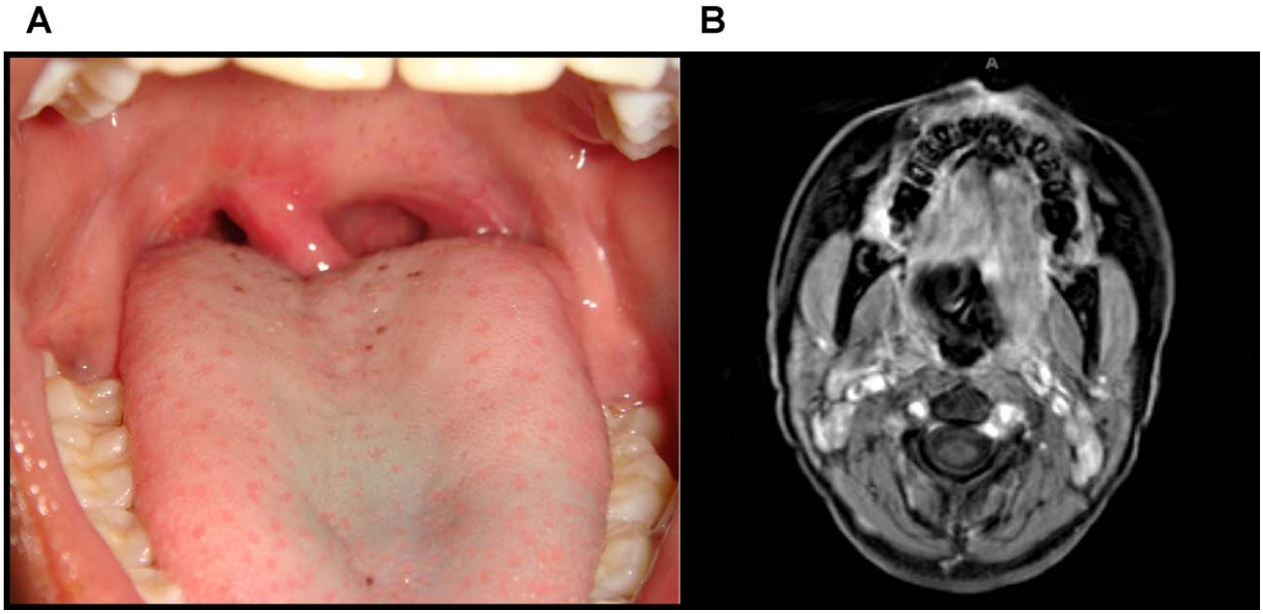

Fig. 5. Postoperative result, 6 months after surgery. (A) Shows the clinical evaluation of the soft palate. The uvula has lateralized to the right due to scar contraction. (B) Shows a T1 weighted MRI with gadolinium with postoperative artifact at the level of right soft palate. No evidence of recurrence seen.

and inhibits *TP53* promoting cell cycle progression [21]. Occasionally, lipoblastomas have a plexiform vascular pattern, a finding also seen in myxoid liposarcoma making adequate diagnosis challenging [5].

3.1.3. Lipomas

Sixty percent of lipomas have rearrangements of chromosome 12q13-15 targeting the HMGIC gene [22]. HMGIC encodes a DNA binding protein which up regulates the growth and differentiation of mesenchymal cells [23]. Less frequently, a deletion of 13q or a rearrangement of 6p21-22 has been reported [24].

3.1.4. Hibernomas

Lipomatous lesions with brown fat differentiation are classified as hibernomas. Typically, hibernomas are asymptomatic and slow growing. Alteration in regions 11q13 and 10q22 are common in these lesions [17,25].

In the present case, we describe a tumor with lobular lesions, fibrous septa and frequent lipoblasts consistent with the classic histological presentation of lipoblastoma. On karyotype and FISH analysis, no abnormalities for chromosome 8 were encountered. Translocations between chromosome 1 and 2 and a 3–6 ring chromosome were identified in the tumor. Alterations in chromosome 1 and 2 have been occasionally reported in hibernomas and other benign soft tissue tumors such as uterine leiomyomas [21,26]. Ring and marker chromosomes are considered non-specific findings, which have been seen in atypical lipomas and well-differentiated liposarcomas [17,23]. We were unable to identify the genetic material in the aberrant ring and marker chromosomes. Specifically, no material from chromosomes 8 was detected.

Although the definitive treatment for lipoblastoma is complete resection with negative margins, tumor recurrence has been reported in 13–20% of the patients [27]. Late recurrences are not uncommon and lesions recurring 10 years after initial resection have been reported [16]. Although lipoblastomas might evolve into mature fat and involute with aging, the recurrence rate of these lesions suggests long-term surveillance is necessary.

4. Conclusion

We report an interesting case of a recurrent lipoblastoma arising in the soft palate of an 8-year-old girl. Cytogenetic analysis of the tumor revealed absence of chromosome traditional 8 abnormalities, and the presence of translocations of chromosomes 1–2, a 3–6 ring chromosome, and a marker chromosome. The traditional morphologic appearance of the tumor and the absence of malignant features suggestive of liposarcoma give added confidence of the diagnosis of lipoblastoma. Due to the relatively high recurrence rate of lipoblastomas, surveillance is recommended.

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